

22

DID THE ADDITION OF CHEMOTHERAPY TO CONVENTIONAL RADIOTHERAPY IMPROVE OUTCOMES IN TREATMENT OF OROPHARYNX CANCER IN ONTARIO, CANADA - A MARKER-TREATMENT INTERACTION STUDY?

Stephen Hall¹, Fei-Fei Liu², Brian O'Sullivan², Patti Groome¹, Willa Shi²

¹Queen's University, Kingston, ON

²University of Toronto, Toronto, ON

Purpose: In 2001 the management of head and neck cancer abruptly changed with the addition of concurrent chemotherapy to radiotherapy based on randomized trials and meta-analyses. The role of Human Papilloma Virus (HPV) and its prognostic impact were subsequently identified in 2004. However there is no evidence on the efficacy of concurrent chemoradiotherapy (CRT) specifically for HPV positive or negative patients over conventional radiotherapy (RT). The objective of this study was to compare treatment effectiveness by HPV status based on a group of patients including those treated before and after CRT was adopted across the cancer centres of Ontario, Canada.

Methods and Materials: A treatment-effectiveness and marker-treatment interaction study of OPC patients treated for cure in 1998, 1999, 2003 and 2004 from all treatment centres in Ontario who had available tissue for HPV testing. The patients were identified using the Ontario Cancer Registry and all charts were reviewed for demographic, patient, treatment and outcome factors. 865 patients were treated for cure and tissue was available on 610. Samples were tested for p16 and if negative were tested again using in-situ hybridization for HPV p16/18 viral DNA. We compared the survival of patients by HPV status and by treatment (RT versus CRT) using the Kaplan-Meier method and Cox Multiple Hazards regression models.

Results: There were 392 HPV positive patients and 199 of the 610 were treated with CRT. The HPV positive patients had 40% better overall survival (OS) and CRT improved OS by 15% over RT alone. However, there was no difference in OS comparing CRT to RT alone for the HPV positive patients (log rank $p = 0.57$) or for the HPV negative group ($p = 0.15$). When the multiple variable analysis was performed including HPV status and the interaction term with treatment, the HR for treatment (RT versus CRT) for HPV positive was 1.003 and for HPV negative was 1.036, and the p value for the interaction term was 0.91 indicating an outcome driven by HPV status not treatment type.

Conclusions: In this study of real-world patients what appeared to be improvement in OS with the addition of concurrent chemotherapy to conventional radiotherapy was confounded by HPV status.

23

IMPACT OF TUMOUR VOLUME AND THE SURROGATE EFFECT OF LYMPH NODE LOCATION ON THE RISK OF DISTANT METASTASIS IN NASOPHARYNGEAL CANCER

Shrinivas Rathod, Shao Hui Huang, Jie Su, John Kim, John Waldron, Andrew Bayley, John Cho, Meredith Giuliani, Andrew Hope, Jolie Ringash, Aaron Hansen, David Goldstein, Li Tong, Wei Xu, Brian O'Sullivan

Princess Margaret Cancer Centre, University of Toronto, Toronto, ON

Purpose: With the advent of IMRT, distant metastasis (DM) has emerged as the most common cause of death in nasopharyngeal cancer (NPC). Lower neck lymph node (LWLN-LN) involvement is considered a poor prognostic factor and has traditionally been included in the most adverse N-category of the NPC TNM classification. NPC tends not to develop isolated spread to discontinuous lymph node (LN) echelons and LWLN-LN may correspondingly represent a continuum in the total burden of lymph node disease. This study evaluates whether tumour volume and the presence of LWLN-LN have independent influence on DM of NPC.

Methods and Materials: All newly diagnosed NPC treated with IMRT +/- chemotherapy from 2005-2013 were reviewed. Primary

(GTV-T) and nodal (GTV-N) volumes were delineated during IMRT treatment and subjected to institutional peer review. LWLN-LN was defined as level IV/Vb (any extension below the caudal border of the cricoid cartilage) based on the recently proposed 8th edition TNM for NPC (Pan JJ, et al., Cancer 2016; 122(4):546-58). Univariate (UVA) and multivariate (MVA) analyses was performed to evaluate prognostic significance of GTV-T, GTV-N and LWLN-LN for DM for the entire and LN-positive (N+) cohort. **Results:** A total of 344 NPC were identified including 52- N0, 87- N1, 158- N2, 16- N3a, and 31- N3b by 7th edition TNM. Median GTV-T was 25 cc (range: 1-253) and GTV-N was 14 cc (range: 0-685). LWLN-LNs were present in 68 (19.7%) cases, all of which also had LNs in the upper neck. LWLN-LN were associated with higher GTV-N ($p < 0.01$). Median follow up was 5.6 years. In UVA, higher GTV-T (< 25 versus ≥ 25 cc) was associated with inferior five-year distant control (DC) [96% versus 78%; $p < 0.001$]. Higher GTV-N (< 14 versus ≥ 14 cc) was also associated with inferior five-year DC [92% versus 82%; $p = 0.02$]. Presence of LWLN-LN was associated with inferior five-year DC [90% versus 75%; $p < 0.01$]. MVA for DC showed that GTV-T [HR: 1.07 (1 -1.13), $p < 0.01$], GTV-N [HR: 1.1 (1.06-1.13), $p = 0.03$] and T classification [HR: 2.71 (1.26 -5.83), $p = 0.01$] were prognostic while LWLN-LN was not [HR: 1.27 (0.65-2.47), $p = 0.48$]. Identical analyses confined to the N+ subset also confirmed the same findings that GTV-T [HR: 1.08 (1 -1.16), $p = 0.04$], GTV-N [HR: 1.09 (1.05-1.13), $p < 0.001$] and T classification [HR: 2.36 (1.03 -5.40), $p = 0.04$] were prognostic for DC but LWLN-LN was not [HR: 1.31 (0.67-2.58), $p = 0.43$].

Conclusions: This study shows that primary and nodal volume are both prognostic for risk of DM after accounting for T and N classification. LWLN-LN has no apparent effect on DM risk after accounting for tumour volume, suggesting LWLN-LN is likely a surrogate of higher nodal volume rather than related to its anatomic location.

24

REDUCTION IN RADIOTHERAPY DOSE TO THE SUBMANDIBULAR GLAND IN PATIENTS WITH ORAL CAVITY CANCER USING A NOVEL SURGICAL TECHNIQUE AND IMRT

Sarah Baker, Jeffson Chung, Han Zhang, Scott Murray, Youness Elkhalidy, Hani Almarzouki, Naresh Jha, Brock Debenham, Hadi Seikaly, Rufus Scrimger

University of Alberta, Edmonton, AB

Purpose: Surgical transfer of the submandibular gland to the submental space in patients with non-oral head and neck cancer prior to adjuvant radiotherapy (RT) has previously been found to reduce the incidence of long-term xerostomia. Patients with oral cavity cancer are not candidates for the traditional submandibular gland transfer (SGT), as the submental space is commonly irradiated. A modified submandibular gland transfer (mSGT) technique was developed in which the contralateral gland is transferred to the peri-parotid space, lateral to the mandible. This study aimed to determine if the dose reduction to the submandibular gland achieved with mSGT results in mean doses below commonly accepted dose constraints, potentially reducing rates of longterm xerostomia.

Methods and Materials: Sixteen consecutive patients with indications for adjuvant RT following surgery were enrolled. The mSGT was carried out at the time of oncologic resection. For each patient, a planning CT scan was performed and a RT plan was generated for volumetric-modulated arc therapy, with conformal avoidance of the transferred gland and parotid if the contralateral neck was pN0. The dose prescribed was 60 Gy in 30 fractions to the tumour bed and involved nodal regions and 54 Gy in 30 fractions to areas at risk of subclinical spread. Doses to the transferred gland and its original location in the submandibular triangle were compared.

Results: In all patients the submandibular gland could be successfully transferred and adjuvant RT delivered according to protocol. The median dose to the transferred submandibular gland was 26.30 Gy (Range: 8.78 to 56.23 Gy) which was significantly lower than the median dose of 55.56 Gy to the